

What is claimed is:

1. An isolated costimulating molecule
 - a) having the biological activity of costimulation of T cells,
 - b) which occurs on activated CD4⁺ and CD8⁺ T lymphocytes but not resting or activated B cells, granulocytes, monocytes, NK cells or dendritic cells, and
 - c) which has two polypeptide chains, the said molecule having a molecular weight of about 55 to 60 kDa determined in a nonreducing SDS polyacrylamide gel electrophoresis, and the two polypeptide chains of the said molecule having a molecular weight of about 27 kDa and about 29 kDa measured in a reducing SDS polyacrylamide gel electrophoresis.
2. An isolated costimulating molecule having the biological activity of costimulation of T cells comprising an amino-acid sequence which shows at least 40% homology with the sequence comprising 199 amino acids in Fig. 15 (SEQ ID NO:2), or a biologically active fragment or an analogue thereof.
3. An isolated costimulating molecule having the biological activity of costimulation of T cells according to claim 2 and comprising the amino acid sequence shown in Fig. 15 (SEQ ID NO:2), or a biologically active fragment or an analogue thereof.
4. An isolated DNA molecule which encodes a costimulating molecule according to claim 1 or a fragment thereof.
5. An isolated DNA molecule which encodes a costimulating molecule according to claim 2 or a fragment thereof.
6. An isolated DNA molecule encoding a costimulating molecule having the biological activity of costimulation of T cells, the sequence being selected from the group consisting of:
 - a) the DNA sequence shown in SEQ ID NO:1 (Fig. 16) and its complementary strand

- b) DNA sequence hybridizing with the sequences in (a) and
- c) DNA sequences which, because of the degeneracy of the genetic code, hybridize with the sequences in (a) and (b).

7. An isolated plasmid or a viral DNA vector comprising a DNA sequence according to claim 4.

8. An isolated plasmid or a viral DNA vector comprising a DNA sequence according to claim 5.

9. A prokaryotic or eukaryotic host cell stably transformed or transfected with a plasmid or DNA vector according to claim 4.

10. A prokaryotic or eukaryotic host cell stably transformed or transfected with a plasmid or DNA vector according to claim 5.

11. Method for preparing a costimulating molecule according to claim 1, comprising the cultivation of the host cell according to claim 9 for expression of the said molecule in the host cell.

12. Method for preparing a costimulating molecule according to claim 1, comprising the cultivation of the host cell according to claim 10 for expression of the said molecule in the host cell.

13. Method for preparing a costimulating molecule according to claim 2, comprising the cultivation of the host cell according to claim 9 for expression of the said molecule in the host cell.

14. Method for preparing a costimulating molecule according to claim 2, comprising the cultivation of the host cell according to claim 10 for expression of the said molecule in the host cell.

15. An antibody which binds a costimulating molecule according to claim 1.
16. An antibody which binds a costimulating molecule according to claim 2.
17. An antibody according to claim 15, which is a monoclonal antibody.
18. An antibody according to claim 16, which is a monoclonal antibody.
19. A monoclonal antibody which specifically recognizes a costimulating molecule according to claim 1, characterized in that B cells of mice which are immunized with human T lymphocytes activated PMA and the Ca^{2+} ionophore ionomycin are fused with a myeloma cell line to give an antibody-secreting hybridoma, and the monoclonal antibodies are purified in flow cytometry for 2-signal molecule-activated against resting T cells.
20. A monoclonal antibody which specifically recognizes a costimulating molecule according to claim 2, characterized in that B cells of mice which are immunized with human T lymphocytes activated PMA and the Ca^{2+} ionophore ionomycin are fused with a myeloma cell line to give an antibody-secreting hybridoma, and the monoclonal antibodies are purified in flow cytometry for 2-signal molecule-activated against resting T cells.
21. A hybridoma cell which generates the monoclonal antibody according to claim 15.
22. A hybridoma cell which generates the monoclonal antibody according to claim 16.
23. Use of substances which inhibit the biological activity of a costimulating molecule according to claims 1 as pharmaceuticals.
24. Use of substances which inhibit the biological activity of a costimulating molecule according to claims 2 as pharmaceuticals.
25. Use according to claim 23, where the substances comprise a monoclonal antibody, natural or synthetic ligands, agonists or antagonists.

26. Use according to claim 24, where the substances comprise a monoclonal antibody, natural or synthetic ligands, agonists or antagonists.

27. Use of substances which inhibit the biological activity of a costimulating molecule according to claim 1 for the production of a pharmaceutical for the treatment of autoimmune diseases, for the prevention of rejection reactions in organ transplants and for the treatment of dysregulation of the immune system.

28. Use of substances which inhibit the biological activity of a costimulating molecule according to claim 2 for the production of a pharmaceutical for the treatment of autoimmune diseases, for the prevention of rejection reactions in organ transplants and for the treatment of dysregulation of the immune system.

29. Use of a costimulating molecule according to claim 1 as pharmaceuticals.

30. Use of a costimulating molecule according to claim 2 as pharmaceuticals.

31. Use of a costimulating molecule according to claim 1 for the production of pharmaceuticals for the treatment of cancers, Aids, asthmatic disorders and chronic viral diseases such as HCV and HBV infections.

32. Use of a costimulating molecule according to claim 2 for the production of pharmaceuticals for the treatment of cancers, Aids, asthmatic disorders and chronic viral diseases such as HCV and HBV infections.

33. Use of cells comprising a costimulating molecule according to claim 1 as pharmaceuticals.

34. Use of cells comprising a costimulating molecule according to claim 2 as pharmaceuticals.

35. Use of cells according to claim 33 for the production of a pharmaceutical for the treatment of cancers, Aids, asthmatic disorders and chronic viral diseases such as HCV and HBV infections.

36. Use of cells according to claim 34 for the production of a pharmaceutical for the treatment of cancers, Aids, asthmatic disorders and chronic viral diseases such as HCV and HBV infections.

37. Use of substances which specifically recognize a costimulating molecule according to claim 1 for the diagnosis of disorders in which the immune system is involved.

38. Use of substances which specifically recognize a costimulating molecule according to claim 2 for the diagnosis of disorders in which the immune system is involved.

39. Use according to claim 37, where the substances comprise nucleic acid (RNA, DNA) molecules.

40. Use according to claim 38, where the substances comprise nucleic acid (RNA, DNA) molecules.

41. Use according to claim 37, where a hybridization or nucleic acid application technique (for example PCR) is used for the diagnosis.

42. Use according to claim 38, where a hybridization or nucleic acid application technique (for example PCR) is used for the diagnosis.

43. Use according to claim 37, where the substances comprise a monoclonal antibody, natural and synthetic ligands, agonists and antagonists.

44. Use according to claim 38, where the substances comprise a monoclonal antibody, natural and synthetic ligands, agonists and antagonists.

45. Use according to claim 37, where an ELISA detection, flow cytometry, Western blot, radioimmunoassay, nephelometry and a histochemical staining is used for the diagnosis.

46. Use according to claim 38, where an ELISA detection, flow cytometry, Western blot, radioimmunoassay, nephelometry and a histochemical staining is used for the diagnosis.

47. Use of substances which have a positive or negative effect on (modulate) the signal transduction pathway of a costimulating molecule according to claim 1 into the T cell as pharmaceuticals.

48. Use of substances which have a positive or negative effect on (modulate) the signal transduction pathway of a costimulating molecule according to claim 2 into the T cell as pharmaceuticals.

49. Use of substances which prevent the up-regulation of a costimulating molecule according to claim 1 on the T-cell surface as pharmaceuticals.

50. Use of substances which prevent the up-regulation of a costimulating molecule according to claim 2 on the T-cell surface as pharmaceuticals.

51. Use of a costimulating molecule according to claim 1 for producing antibodies.

52. Use of a costimulating molecule according to claim 2 for producing antibodies.

53. A polypeptide constituting a cell surface molecule having characteristics below:

- a) said cell surface molecule is expressed in at least thymocytes and mitogen-stimulated lymphoblast cells;
- b) an antibody reactive to said cell surface molecule induces adhesion between mitogen-stimulated lymphoblast cells;
- c) an antibody reactive to said cell surface molecule induces proliferation of peripheral blood lymphocytes in the presence of an antibody against CD3;

- d) said cell surface molecule has a partial amino acid sequence represented by Phe-Asp-Pro-Pro-Phe in its extracellular region; and
- e) said cell surface molecule has a partial amino acid sequence represented by Tyr-Met-Phe-Met in its cytoplasmic region.

54. The polypeptide of claim 53, comprising the amino acid sequence of SEQ ID NO: 2 or the amino acid sequence of SEQ ID NO: 2 in which one or more amino acids are substituted, deleted, or added.

55. The polypeptide of claim 53, which is encoded by a DNA hybridizing with a DNA having the nucleotide sequence of SEQ ID NO: 1 under stringent conditions.

56. The polypeptide of claim 53, comprising an amino acid sequence having 60% or more homology with an amino acid sequence of SEQ ID NO: 2.

57. A gene encoding the polypeptide of claim 53.

58. The gene of claim 57, wherein said gene is a cDNA.

59. The gene of claim 58, wherein said cDNA has a nucleotide sequence of SEQ ID NO: 1.

60. The gene of claim 58, wherein said cDNA comprises a nucleotide sequence corresponding to nucleotide residues 68 to 667 of SEQ ID NO: 1.

61. A vector comprising the gene of claim 57.

62. A transformant into which the vector of claim 61 has been introduced.

63. A polypeptide fragment comprising an extracellular region of the polypeptide of claim 53.

64. A gene encoding the polypeptide fragment of claim 63.

65. A homodimer molecule comprising two polypeptide fragments, wherein each of the fragments comprises an extracellular region of the polypeptide of claim 53 and said two polypeptide fragments bridged through disulfide bonds to each other.

66. A pharmaceutical composition comprising the polypeptide fragment of claim 63 and a pharmaceutically acceptable carrier.

67. A fusion polypeptide comprising an extracellular region of the polypeptide of claim 1.

68. A homodimer molecule comprising two fusion polypeptides of claim 67, wherein the two polypeptides bridged through disulfide bonds to each other.

69. A pharmaceutical composition comprising either of the fusion polypeptide of claim 67 and a pharmaceutically acceptable carrier.

70. The pharmaceutical composition of claim 69, wherein said pharmaceutical composition is utilized for treating autoimmune diseases or allergic diseases, or for preventing said disease symptom.

71. An antibody or a portion thereof reactive to the polypeptide of claim 53, or the cell surface molecule comprising said polypeptide.

72. The antibody of claim 71 or a portion thereof, wherein said antibody is a monoclonal antibody.

73. A monoclonal antibody or a portion thereof reactive to the polypeptide having an amino acid sequence of SEQ ID NO: 2, the polypeptide fragment of claim 63, or the cell surface molecule comprising said polypeptide.

74. A pharmaceutical composition comprising the monoclonal antibody of claim 73 or a portion thereof and a pharmaceutically acceptable carrier.

75. The pharmaceutical composition of claim 74, wherein said pharmaceutical composition is utilized for treating autoimmune diseases or allergic diseases, or for preventing said disease symptom.

76. A hybridoma producing the monoclonal antibody of claim 72.